ANTIBIOTIC METAPHYLAXIS TO CONTROL RESPIRATORY DISEASE

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Overview

Metaphylaxis (mass medication) to manage respiratory disease in newly received high stress or recently weaned cattle has been a common practice.[37] The beef industry's use of antibiotics is coming under more and more scrutiny. The Food and Drug Administration (FDA) and Center for Disease Control (CDC) have on going epidemiologic studies to assess antibiotic resistance among human bacterial pathogens and the relationship to agricultural use of antibiotics. It is very possible many of the antibiotics cattlemen rely on today will be lost in the future. For this reason it becomes very important for cattlemen to carefully consider how they select and use antibiotics. See "A Producers Guide for Judicious Use of Antimicrobials in Cattle", figure 1.

The questions that must be addressed when considering antibiotic metaphylaxis or mass medication of newly received high stressed or recently weaned cattle include: What is the probability the group of cattle being considered for metaphylactic antibiotic use will have a high rate of bacterial respiratory disease? Are there any management techniques other than metaphylactic use of antibiotics that will reduce the pending respiratory disease in the newly received group of cattle to a manageable level? Will antibiotic metaphylaxis prevent or reduce the respiratory sickness and death loss in newly purchase commingled high stressed cattle? And if so will the reduction in health problems be significant to warrant the use of an antibiotic metaphylacticly? Will the reduction in suffering caused by respiratory disease be great enough to off set the cost of antibiotic metaphylaxis? Will the use of antibiotic metaphylaxis decrease the response seen to antibiotics in future cases of respiratory disease in cattle in the group treated with antibiotics metaphylacticly? Will the long term effects on bacterial antibiotic resistance make it difficult to treat future cases of bacterial disease in your cattle or humans working round the cattle? This paper will attempt to address these questions. .

Introduction

Respiratory disease is most often diagnosed during the first four weeks of the feeding period. Consistent prevention and / or control is difficult and costly. Several viruses and bacteria have been associated with acute bovine respiratory disease (BRD). Individually, these pathogens do not appear to be capable of causing disease in healthy cattle. Interactions among the respiratory pathogens and compromise of the innate respiratory defense mechanisms, especially as a result of environmental and management stresses such as heat or cold and weaning and transportation, seems to be critical to the development of clinical BRD [2] BRD in post-weaned cattle is seldom recognized as a disease entity caused by a single pathogen[6]. Management strategies that focus on pre-weaning immunizations, minimizing transportation stress and prophylactic / metaphylactic (mass medication) antibiotic treatment have yielded the most cost effective results in controlling weaning associated BRD.[4, 17, 19, 22, 35]

First Question: What is the probability the group of cattle being considered for metaphylactic antibiotic use will have a high rate of bacterial respiratory disease?

The answer must include an understanding of BRD as a syndrome. Interactions among respiratory pathogens and compromise of the innate respiratory defense mechanisms, due to environmental, nutritional and management stressors seems to be critical to the development of clinical BRD.[2, 4, 17]

Environmental stresses include heat or cold stress, respirable dust, and fumes toxic to the respiratory epithelium.[27] Management stresses that lead to dehydration and increased levels of circulating glucocortioids play an important role in disarming an animal's respiratory defense mechanisms.[27, 33, 38, 39] Once the innate defense mechanisms are disarmed, potential bacterial pathogens that normally reside in the upper respiratory tract are allowed access to the

lung.[5, 8, 9 10, 11, 12, 18, 40] An aerosol of pathogenic respiratory bacteria has been shown to make cattle susceptible to respiratory viral infection. Therefore it should not be supposed that the bacterial component of BRD necessarily follows a viral infection.[17]

High stressed, newly weaned cattle have a long history for suffering from high sickness and death rates.[17, 34, 35, 37, 38] Morbidity rates are commonly reported to be in excess of 50% of received cattle.[4,15, 34]

A Long list of viruses associated with BRD:

- Bovine herpes virus 1 and 3 (IBR)
- Bovine parainfluenza 3 virus (Pl3)
- Bovine viral diarrhea virus (BVDV)
- Bovine respiratory syncytial virus (BRSV)
- Bovine adenovirus
- Bovine rhinovirus
- Bovine coronavirus

IBR, Pl3, BVDV, and BRSV are the common viruses associated with acute BRD.[1] Respiratory disease caused by these viruses can occur without significant interaction with other pathogens. These are also the only viral pathogens for which a vaccine is available. However, viral vaccination has been shown to be protective against experimentally induced bacterial pneumonia.[17, 34, 35] Viral vaccination in the Texas A&M Value Added Calf (VAC) Program prior to weaning has been shown to be effect in controlling weaning related BRD.[22]

Second Question: Are there any management techniques other than metaphylactic use of antibiotics that will reduce the pending respiratory disease in the newly received group of cattle to a manageable level?

When purchasing cattle from sources known for delivering commingled high stress cattle, every effort should be made to ensure the cattle are handled with care and shipped to your location as quickly as possible. Once the cattle arrive there is little you can do to manage the events of the past, but handling with care after arrival should decrease the additive stresses associated with BRD development.[6, 21, 26]

Arrival Handling Check List

- Employee training. Don't take for granted the people you have helping you know how you want cattle handled or how products should be used. Regular training in good management practices is available from your cattlemen's association and extension service.
- Be prepared. Visit with your veterinarian and set up a processing schedule appropriate to the needs of the cattle. Have all supplies in stock. These include clean water, fresh clean feed, properly handled vaccines, sterile needles and syringes.
- Protect newly received cattle. Cattle are very susceptible to environmental stress. Providing shade in hot weather and windbreaks in cold weather will decrease environmental stress.
- Timing. When the ambient temperature is predicted to be above 80 degrees, time processing to be completed and have the cattle in their home pen early in the day before the day's temperature reaches 80 degrees.
- Keep the cattle calm. Loud noises, hot shots and rough handling increase the animal's cortisol blood level. Cortisol decreases the immune response and innate disease defense mechanisms. Rough handling will not only decrease the value of vaccines but increase the observe incidence of BRD.
- Observe cattle closely. Check cattle closely multiple times a day for early signs of disease and/or injury. Early detection of BRD is crucial to successful treatment.

Vaccination of high stressed cattle on arrival with a viral modified live vaccine that includes IBR, BVD, PI3 and/or BRSV is believed to reduce BRD incidence and severity.[17, 35] As much as a 50% reduction in BRD incidence has been reported.[17] Killed modern sub-unit vaccines for *Mannheimia haemolytica* (previously known as *Pasteurella haemolytica*) are thought to be effective if given well in advance of situations and stressors that lead to BRD but have little benefit if given at processing of newly received commingled high stress cattle.[17] Modern modified live vaccines that contain both *Mannheimia haemolytica* and *Pasteurella multocida* may hold more promise for use at arrival. Few

studies are available to definitively support the value of vaccines in controlling respiratory disease in high stress cattle. [26]

Third Questions: Will antibiotic metaphylaxis prevent or reduce the respiratory sickness and death loss in newly purchase commingled high stressed cattle? And if so will the reduction in health problems be significant to warrant the use of an antibiotic metaphylacticly?

Antibiotics have no effect on respiratory viral pathogens and since viruses are the principle pathogenic instigators of BRD at first glance antibiotics given in the early stages of BRD might not be considered reasonable.

Metaphylactic use of antibiotics in high stress commingled within 72 hours of arrival have consistently proven to effective in decreasing both morbidity and mortality associated with BRD. [36] And as one would expect when animal suffering is reduced the animals growth improves. These trials included the injectable use of Ceftiofur (Naxcel & Excenel), Florfenicol (Nuflor), long-acting Oxytetracycline, and Tilmicosin (Micotil) and the use of feed chlortetracycline and sulfamethazine. [13, 14, 20, 23, 24, 31, 32] Additionally, data, much of which dates back over 30 years, has shown metaphylactic antibiotic use consistently lower morbidity and mortality associated with weaning related BRD. [17] These trials reported a 20% to 44% reduction in sickness rate and a 0% to 24% reduction in death loss. [13, 14, 20, 23, 24, 31, 32]

The bacteria involved and antibiotic selection

First consider the bacteria involved and the role they play in BRD. In general, bacteria do not serve as primary pathogens of BRD in healthy, unstressed cattle. The bacteria and bacteria-like agents that have been most commonly associated with this disease complex include:

- *Mannheimia haemolytica* (previously known as *Pasteurella haemolytica*)
- *Pasteurella multocida*
- *Hemophilus somnus*
- *Mycoplasma* spp.
- *Chlamydia* spp.

Mannheimia haemolytica type Al is commonly isolated from fatal cases of BRD. [3, 9, 10, 12] *Pasteurella multocida* is believed to cause less fulminating respiratory disease but is reported more often than *M. haemolytica*. *P. multocida* may be more important in BRD of younger feeder cattle. [15] *Hemophilus somnus* is reported more commonly in fatal cases of BRD in the colder climates of North America. This observation has created controversy about the role of *H. somnus* in BRD in moderate climates. [17] Discrepancies in isolation rates of fatal cases of BRD may not be associated with climatic differences. Differences in livestock genetics and production practices among regions may be associated with the reported isolations of the organism. [17] *Mycoplasma bovis* is commonly isolated by some diagnostic laboratories. While this organism is not considered a primary pathogen in weaned or yearling cattle, a *Mycoplasma*-like lesion is frequently observed in finished cattle at the packing plant. [17] These organisms are often isolated in association with other bacterial respiratory pathogens, and their role in BRD may be interactive with other pathogens. [35] Vaccines have either been ineffective or have made *Mycoplasma* related BRD worse. [17, 35] Prophylactic antibiotic use has not consistently been reported to change the incidence of *Mycoplasma* isolation or severity of *Mycoplasma* lesions. [7, 24]

Cattle as prey animals are extremely good at hiding their symptoms. Clinical signs develop within 14 days but because of the multitude of etiologic factors involved the clinical signs may vary. [16, 17] Generally clinical signs include loss of appetite, rapid respiration, generalized depression and weakness, coughing, increased nasal and ocular discharge, stiff movement and shorten stride, and high body temperatures. [35] The onset can be very dramatic, with the occasional animal found dead and a large percentage of cattle in a group showing severe depression. [7, 17,] The value of metaphylactic antibiotics in part is related to ability of cattle to hide symptoms and the explosive nature of the bacterial phase of BRD once viral damage has cripple the bacterial defense mechanisms in the upper respiratory tract. The decrease in the potential pathogenic bacterial populations in the upper respiratory region by metaphylactic antibiotic use may be related to the improve health parameters observed. [2, 4, 8, 10] Additionally, metaphylactic

antibiotics may decrease the role of bacteria such as *M. bovis* that are marginally pathogenic but that may have a significant additive effect in BRD development.

Metaphylactic antibiotic selection should be discussed with your veterinarian. Your veterinarians will consider age and source of the cattle, the type of stress the cattle will endure and previous laboratory antibiotic sensitivities for isolated bacterial pathogens.[3, 30] There are some antibiotics that should never be considered for metaphylactic use. These include; injected gentamicin, injected neomycin, and enrofloxacin (Baytril). Additionally, cattlemen must understand it is a violation of federal law to use antibiotics other than as directed on the label unless prescribed by a veterinarian. Before writing a prescription, federal law requires a veterinarian have personal knowledge of the cattle and their management, determine that use other than as labeled is required, that the veterinarian is available for follow up and the withdrawal time is significantly extended so that no violative residues will be found.

Forth Question: Will the reduction in suffering caused by respiratory disease be great enough to off set the cost of antibiotic metaphylaxis?

Detailed breakeven analysis of the cost of BRD shows reduction from 30% sickness to 20% sickness will be worth approximately 4% additional cattle purchase price in health cost savings. Cattlemen commonly fall for this trap. When breakeven analysis considers performance losses over the backgrounding period the value appears to be worth an additional 4% or about $4.00 per CWT. Less data is available for analysis of performance loss for the entire feeding period, but suggests losses will cost in excess of 30 pounds gain and a 2% decrease in carcass value.[16, 28, 29, 36]

Fifth Question: Will the use of antibiotic metaphylaxis decrease the response seen to antibiotics in future cases of respiratory disease in cattle in the group treated with antibiotics metaphylacticly?

Few studies are available to answer this important question. But the available data suggest metaphylactic antibiotic use does not alter the effectiveness of the medication if used on clinical BRD cases from the same group.[23, 38]

Sixth Question: Will the long term effects on bacterial antibiotic resistance make it difficult to treat future cases of bacterial disease in your cattle or humans working round the cattle?

Data available for BRD bacterial pathogens does not support observations of significant changes in the antibiotic resistance pattern. Perhaps this is because BRD bacterial pathogens tend to be kept isolated within groups of cattle and terminate at the packers.

The FDA and CDC are very concerned about antibiotic resistance in animal pathogens such as *Salmonella* that could be transferred to humans. For the past few years a national antibiotic resistance monitoring program has been in place but little is presently available to support a relationship. The FDA has initiated a new “Framework” for evaluating antibiotics that are cleared for use in agriculture. The new approach to antibiotic approval considers the significance of an antibiotic for treatment of human disease and the duration the antibiotic is typically used. Pharmaceutical companies are now required to continually monitor antibiotic resistance changes. It has become very important for cattlemen to work with their veterinarian when selecting and using antibiotics and to adopt judicious antibiotic use guidelines.